REMARKS

Status of the Claims

Claims 1-5, 7-15, 17, 37-42 are pending herein, claims 6, 16 and 18-36 having been deleted without prejudice and claims 37-42 having been added.

A separate sheet entitled "**Version with Markings to Show Changes Made**" is provided to illustrate the deletion of claims 6, 16 and 18-36 without prejudice, the addition of claims 37-42, and the amendment of claims 1, 2, 4, 7-12 and 17. Unamended claims are also included for the Examiner's convenience.

Support for polymer microparticles in claim 1 can be found, for example, in originally filed claim 8.

Support for an incompatible component of a pharmaceutical article can be found, for example, in paragraph [0022] of the specification.

Support for commingled pharmaceutically active agent and polymer microparticles can be found, for example, in paragraph [0045] of the specification.

Support for latex beads can be found, for example, in paragraph [0032] of the specification.

Support for polymer microparticles provided in an amount of 0.01 to 10 wt% in suspension can be found, for example, in paragraph [35] of the specification.

Support for a drug delivery medical device component as an incompatible component can be found, for example, in paragraph [0050] of the specification.

Support for a catheter as a drug delivery medical device can be found, for example, in paragraph [0052] of the specification.

Support for a needle injection catheter can be found, for example, in paragraph [0052] of the specification.

Support for a needle injection catheter that is adapted for endocardial, epicardial, or pericardial administration can be found, for example, in paragraph [0052] of the specification.

Support for a medical device for parenteral injection can be found, for example, in paragraph [0051] of the specification.

Response to Office Action

Responsive to the Office Action mailed October 24, 2002 in the above matter, please consider the following remarks.

A. Rejection of Claims 1-3 and 7-17 under 35 U.S.C. 112, first paragraph, Written Description.

Claims 1-3 and 7-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time that the application was filed, had possession of the claimed invention. The Office Action states *inter alia,* that "[t]he skilled artisan cannot envision the detailed structure of a genus of the claimed *microparticles* and/or *components* for use within the context of the claimed invention..." Office Action, page 4 (emphasis added).

The Applicants respectfully traverse this rejection and its supporting remarks.

"To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." See, e.g., MPEP 2163 (Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement).

Although the issue of a lack of adequate written description can arise for an originally filed claim, such situations are unusual. See, e.g., MPEP 2163.03 (emphasis supplied):

> While a question as to whether a specification provides an adequate written description may arise in the context of an original claim which is not described sufficiently (see, e.g., *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997)), ***there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed.*** *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). Consequently, ***rejection of an original claim for lack of written description should be rare.*** Most typically, the issue will arise in the following circumstances: [a] AMENDMENT AFFECTING A CLAIM... [b] RELIANCE ON FILING DATE OF PARENT APPLICATION UNDER 35 U.S.C. 120..., [c] RELIANCE ON PRIORITY UNDER 35 U.S.C. 119... [d] SUPPORT

FOR A CLAIM CORRESPONDING TO ACOUNT IN AN INTERFERENCE.

"*Possession may be shown in many ways*.... A specification may describe an actual reduction to practice *by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim* and determined that the invention would work for its intended purpose...." MPEP 2163 (emphasis added). In this connection, it is noted that the applicants have reduced the present invention to practice. See Example 1 of the present specification.

The Office Action refers to *Feirs* and *Eli Lily*, which are discussed in MPEP 2163 (emphasis added):

> For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. ***Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics*** or combinations of characteristics ***may demonstrate the requisite possession. For example, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may*** be sufficient to show possession of the claimed invention to one of skill in the art. See *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966 ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention"). ***A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is."*** *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)).

However, the presently pending claims are not directed to coding sequences. Nor are the microparticles and components in the claims defined by function alone. For example, claim 1, the only independent claim pending in this application, is presently directed to (a) *polymer* microparticles and (b) a component *of a pharmaceutical article*.

For at least the above reasons, it is respectfully submitted that claims 1-3 and 7-17 are presently in compliance with the written description requirement of 35 U.S.C. 112, first paragraph. Reconsideration and withdrawal of the rejection of these claims on this basis are, accordingly, respectfully requested.

B. Rejection of Claims 1-3 and 7-17 under 35 U.S.C. 112, first paragraph, Enablement.

Claims 1-3 and 7-17 are rejected as not enabled under 35 U.S.C. 112, first paragraph. The Applicants respectfully traverse this rejection and its supporting remarks.

MPEP 2164.04 states that "[i]n order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure)...." Furthermore, the "analysis and conclusion of a lack of enablement are [to be] based on the [*In re* Wands] factors discussed in MPEP § 2164.01(a) and the evidence as a whole, [although] it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims.... [S]pecific technical reasons are always required." *Id.*

The Office Action, on the other hand, merely states that the specification does not reasonably provide enablement for the pending claims, which encompass combinations of microparticles and components other than the allowable combination of suitable polymer microparticles and a medical delivery device. The Office Action further asserts that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Finally, the Office Action concludes that "since the claimed invention is not supported by a sufficient written description (for possessing of the genus of the materials which are necessary for the practice of the claimed invention), particularly in view of the reasons set forth above, one skilled in the art would not know how to use and make the claimed invention so that it would operate as intended." Office Action of October 24, 2002, page 5.

In view of the above, it is respectfully submitted that the Office Action does not focus on the "factors, reasons and evidence," that are required to meet its initial burden to establish a reasonable basis to question the enablement that is provided for the claimed invention.

Moreover, the Office Action appears to suggest that, because the claims embrace a large number of microparticles and incompatible components, an undue amount of experimentation will be required before a person skilled in the art can make and use the invention. However, as noted in paragraph [0025] of the present specification, "[i]t is well within the skill of those of ordinary skill in the art to determine which materials, in addition to those [metallic and polymeric materials] specifically listed above, are incompatible with a given pharmaceutically active agent." Regarding the microparticle materials, see paragraph [0031]: "Those of ordinary skill in the art will be able to determine which polymers are most appropriate for a given pharmaceutically active material with relative ease using, for example, techniques like those used in the Examples."

Indeed, it would be a routine matter for one of ordinary skill in the art to conduct tests to determine (a) which components are incompatible with a pharmaceutically active agent of interest and (b) which microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent that is greater than a pharmaceutical effectiveness of the pharmaceutically active agent in the absence of the microparticles. In this connection, note the following: "'[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance.' *In re Colianni*, 561 F.2d at 224,195 USPQ at 153. 'The test is not merely quantitative, since ***a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.***' *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976))." Excepted from "Training Materials for Examining Patent Applications with Respect to 35 U.S.C. Section 112, First Paragraph-Enablement Chemical/Biotechnical Applications" (emphasis supplied).

For at least the above reasons, reconsideration and withdrawal of the rejection of presently pending claims 1-3 and 7-17 as not enabled under 35 U.S.C. 112, first paragraph are respectfully requested.

C. Rejection of Claims 1-3 and 7-17 under 35 U.S.C. 102(e)--Pinchuk et al.

Claims 1-3 and 7-17 are presently rejected under 35 U.S.C. 102(b) as being anticipated by Pinchuk et al., U.S. Pat. Appln. Pub. No.2002/0107330 ("Pinchuk"). This rejection and its supporting remarks are respectfully traversed.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). See also MPEP 2131.

Presently pending claim 1 is directed to a method of using *polymer microparticles* to protect the pharmaceutical effectiveness of a pharmaceutically active agent. Claim 1 requires that a pharmaceutically acceptable *suspension* be provided, which comprises a pharmaceutically active agent *commingled* with polymer microparticles. The pharmaceutically acceptable suspension is exposed to a component of a pharmaceutical article that is incompatible with the pharmaceutically active agent. Due to the presence of the polymer microparticles in the suspension, the pharmaceutical effectiveness of the pharmaceutically active agent is greater than it would otherwise be in the absence of the polymer microparticles.

Paragraphs [0059] and [0176]-[0178]of Pinchuk referred to in the Office Action concern therapeutic-agent-*loaded* block copolymer compositions for therapeutic agent delivery. Example 2 of Pinchuk discloses the use of *solutions* containing (1) between 0-94%, preferably 94%, toluene, (2) between 5%-99%, preferably 5%, tetrahydrofuran and (3) 1% copolymer and paclitaxel, which are used to provide a therapeutic-agent-loaded block copolymer *layers* on various medical devices.

In contrast to the presently pending claim 1, however, Pinchuk does not appear to disclose (a) providing a pharmaceutically acceptable *suspension* comprising a pharmaceutically active agent polymer microparticles, wherein the *pharmaceutically active agent and polymer microparticles* are *commingled within the suspension*; and (b)

exposing the pharmaceutically acceptable suspension to an incompatible component that is incompatible with the pharmaceutically active agent, wherein the incompatible component is a component of a pharmaceutical article, and wherein the polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent that is greater than a pharmaceutical effectiveness of the pharmaceutically active agent when exposed to the incompatible component in the absence of the polymer microparticles.

Note from paragraph [0033] of the present specification that "microparticles" are small particles ranging in largest dimension from 0.01 to 1000 microns. Note also that, in the present invention, the polymer microparticles and the therapeutic agent are commingled (i.e., combined) in the suspension. The polymer microparticles and the therapeutic agent can be commingled using essentially any known technique, including stirring, shaking, and so forth. See, for example, paragraph [0044] and Example 1 of the present specification.

For at least the above reasons, it is respectfully submitted that claim 1 is not anticipated by Pinchuk. Claims 2, 3, and 7-17, which depend from claim 1, are patentable over Pinchuk for at least the same reasons.

Accordingly, reconsideration and withdrawal of the rejection of claims 2, 3, and 7-17 as being anticipated by Pinchuk are respectfully requested.

The presently pending claims are patentable for similar reasons over Ragheb et al. (U.S. Pat. Appln. No. 2002/0032414) and Shi et al. (U.S. Patent No. 6,004,943), which were stated n the Office Action to be relevant to the present invention, but which were not used to reject the claimed invention.

CONCLUSION

Applicants submit that this application is in condition for allowance, early notification of which is earnestly solicited. The Examiner is encouraged to contact the undersigned at (703) 433-0510 to discuss any outstanding issues in this case.

FEES

The Office is authorized to charge any fees required in connection with this application to deposit account number 50-1047.

Respectfully submitted,

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(Signature)

Version With Markings To Show Changes Made

IN THE CLAIMS:

1. (Amended) A method of using polymer microparticles to protect pharmaceutical effectiveness of a pharmaceutically active agent comprising:

providing a pharmaceutically acceptable suspension comprising a pharmaceutically active agent and polymer microparticles, wherein said pharmaceutically active agent and polymer microparticles are commingled within said pharmaceutically acceptable suspension; and

exposing said pharmaceutically acceptable suspension to an incompatible component ~~or condition~~ that is incompatible with said pharmaceutically active agent, wherein said incompatible component is a component of a pharmaceutical article, and wherein said polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent that is greater than a pharmaceutical effectiveness of the pharmaceutically active agent when exposed to the incompatible component in the absence of the polymer microparticles.

2. (Amended) The method of claim 1, wherein said ~~pharmaceutically acceptable suspension is exposed to a component comprising a metal~~ incompatible component comprises a metal.

3. The method of claim 2, wherein said metal is selected from stainless steel and nickel-titanium superalloy.

4. (Amended) The method of claim 1, wherein said ~~pharmaceutically acceptable suspension is exposed to a~~ incompatible component ~~comprising~~ comprises a polymer.

5. The method of claim 4, wherein said polymer is selected from polyether ether ketone, polyimide, epoxy, nylon, acrylonitrile/butadiene/styrene polymers and polycarbonate.

~~6. The method of claim 1, wherein said pharmaceutically acceptable suspension is exposed to a freeze-thaw cycle.~~

7. (Amended) The method of claim 1, wherein said polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent that is at least 10% greater than a pharmaceutical effectiveness of the pharmaceutically active agent in the absence of the polymer microparticles.

8. (Amended) The method of claim 1, wherein said polymer microparticles ~~are polymer microparticles~~ are latex beads.

9. (Amended) The method of claim 1, wherein said polymer microparticles are polystyrene microparticles.

10. (Amended) The method of claim 1, wherein said polymer microparticles range from 0.01 to 100 microns in largest dimension.

11. (Amended) The method of claim 1, wherein the polymer microparticles range from 0.1 to 10 microns in largest dimension.

12. (Amended) The method of claim 1, wherein the polymer microparticles are provided in an amount of 0.1 to 1 wt% in said suspension.

13. The method of claim 1, wherein the pharmaceutically active agent comprises a polynucleotide.

14. The method of claim 13, wherein the pharmaceutically active agent is a cell, a plasmid or a viral vector.

15. The method of claim 14, wherein the pharmaceutically active agent is a viral vector selected from an adenoviral vector and an adeno-associated viral vector.

~~16. The method of claim 1, wherein said microparticles are polymer microparticles and wherein said pharmaceutically active agent comprises a polynucleotide.~~

17. (Amended) The method of ~~claim 16~~ claim 1, wherein said microparticles are polystyrene microparticles and wherein said pharmaceutically active agent is selected from a cell, a plasmid and a viral vector.

~~18. A method of treatment comprising:~~

~~providing a pharmaceutically acceptable suspension comprising a pharmaceutically active agent and microparticles;~~

~~providing a medical device having a component that is incompatible with said pharmaceutically active agent; and~~

~~parenterally injecting said pharmaceutically active agent into a patient from said device while at the same time removing said microparticles from said pharmaceutically acceptable suspension.~~

~~19. The method of claim 18, wherein said microparticles are polymer microparticles.~~

~~20. The method of claim 18, wherein said microparticles are polystyrene microparticles.~~

~~21. The method of claim 18, wherein the microparticles range from 0.1 to 10 microns in largest dimension.~~

~~22. The method of claim 18, wherein the pharmaceutically active agent comprises a polynucleotide.~~

~~23. The method of claim 22, wherein the polynucleotide is provided within a cell, a plasmid or a viral vector.~~

~~24. The method of claim 18, wherein said device is a parenteral injection device selected from a vascular catheter and a syringe.~~

~~25. A pharmaceutically acceptable suspension comprising:~~

~~a pharmaceutically active agent; and~~

~~microparticles, wherein said microparticles are provided to prevent a substantial reduction in pharmaceutical effectiveness of said pharmaceutically active agent upon being exposed to a material or condition that is incompatible with said pharmaceutically active agent.~~

~~26. The pharmaceutically acceptable suspension of claim 25, wherein said microparticles are polymer microparticles.~~

~~27. The pharmaceutically acceptable suspension of claim 25, wherein said microparticles are polystyrene microparticles.~~

~~28. The pharmaceutically acceptable suspension of claim 25, wherein the microparticles range from 0.1 to 10 microns in largest dimension.~~

~~29. The pharmaceutically acceptable suspension of claim 25, wherein the pharmaceutically active agent comprises a polynucleotide.~~

~~30. The pharmaceutically acceptable suspension of claim 29, wherein the polynucleotide is provided within a cell, a plasmid or a viral vector.~~

~~31. An ampoule containing the pharmaceutically acceptable suspension of claim 25.~~

~~32. A device for parenteral injection comprising:~~

~~a pharmaceutically acceptable suspension comprising a pharmaceutically active agent and microparticles;~~

~~a device component that contacts said suspension and is incompatible with said pharmaceutically active agent; and~~

~~a separator, said separator acting to remove said microparticles from said pharmaceutically acceptable suspension prior to parenteral injection.~~

~~33. The device of claim 32, wherein said microparticles are polymer microparticles.~~

~~34. The device of claim 32, wherein the microparticles range from 0.1 to 10 microns in largest dimension.~~

~~35. The device of claim 32, wherein the pharmaceutically active agent comprises a polynucleotide.~~

~~36. The device of claim 32, wherein said device is a parenteral injection device selected from a vascular catheter and a syringe.~~

37. (Newly Added) The method of claim 1, wherein the polymer microparticles are provided in an amount of 0.01 to 10 wt% in said suspension.

38. (Newly Added) The method of claim 1, wherein said incompatible component is a drug delivery medical device component.

39. (Newly Added) The method of claim 38, wherein said drug delivery medical device is a catheter.

40. (Newly Added) The method of claim 39, wherein said catheter is a needle injection catheter.

41. (Newly Added) The method of claim 40, wherein said needle injection catheter is adapted for endocardial, epicardial, or pericardial administration.

42. (Newly Added) The method of claim 38, wherein said drug delivery medical device is a medical device for parenteral injection.